REVIEW

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REVIEW

Radiation doses and risks from internal emitters

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Abstract
This review updates material prepared for the UK Government Committee Examining Radiation Risks from Internal Emitters (CERRIE) and also refers to the new recommendations of the International Commission on Radiological Protection (ICRP) and other recent developments. Two conclusions from CERRIE were that ICRP should clarify and elaborate its advice on the use of its dose quantities, equivalent and effective dose, and that more attention should be paid to uncertainties in dose and risk estimates and their implications. The new ICRP recommendations provide explanations of the calculation and intended purpose of the protection quantities, but further advice on their use would be helpful. The new recommendations refer to the importance of understanding uncertainties in estimates of dose and risk, although methods for doing this are not suggested. Dose coefficients (Sv per Bq intake) for the inhalation or ingestion of radionuclides are published as reference values without uncertainty.

The primary purpose of equivalent and effective dose is to enable the summation of doses from different radionuclides and from external sources for comparison with dose limits, constraints and reference levels that relate to stochastic risks of whole-body radiation exposure. Doses are calculated using defined biokinetic and dosimetric models, including reference anatomical data for the organs and tissues of the human body. Radiation weighting factors are used to adjust for the different effectiveness of different radiation types, per unit absorbed dose (Gy), in causing stochastic effects at low doses and dose rates. Tissue weighting factors are used to take account of the contribution of individual organs and tissues to overall detriment from cancer and hereditary effects, providing a simple set of rounded values chosen on the basis of age- and sex-averaged values of relative detriment. While the definition of absorbed dose has the scientific rigour required of a basic physical quantity, the same is not true of the ICRP protection quantities equivalent and effective dose (i.e. those measured in sieverts). The ICRP quantities are intended for practical application in radiological protection and the choice of radiation and tissue...
weighting factors used in their calculation involves simplifying assumptions regarded as acceptable for this purpose. Best estimates of doses and risks to individuals and specific population groups may be calculated using ICRP biokinetic and dosimetric approaches, but would require the use of best available information on RBE and age-, sex- and population-specific risk factors.

Consideration of uncertainties is important in applications such as the assessment of the probability of cancer causation for an individual and in estimating doses in epidemiological studies. While the ICRP system of protection does not take explicit account of uncertainties, an understanding of the various contributions to uncertainty can be seen to be of value when making judgments on the optimisation of protection.

1. Introduction

Information on radiation doses in humans, and the risks associated with them, is needed and used for many purposes. Governments wish to establish controls on industries and regulators need to ensure compliance with any limitations which may be set. Scientific investigators, such as epidemiologists and radiation biologists, need to quantify radiation exposures for statistical or mechanistic analyses. Medical practitioners and their patients need to ensure that the gain from radiation-based investigations or interventions is balanced against the potential detriments of radiation exposure. And individual members of the general public may wish (and have the right) to know the risks of radiation exposure from a multiplicity of sources, some voluntary, some involuntary, and to make informed decisions. In each case, a compromise must be reached between the requirements for an accurate and scientifically robust assessment, on the one hand, and the need for an understandable, transparent and reproducible (and hence legally enforceable) methodology on the other. In simple terms, this is a compromise between scientific precision and practicality.

For the specific purposes of radiation protection relating to the induction of cancer and hereditary effects, simplifying assumptions are made that doses calculated for various external and internal sources of radiation can be amalgamated, and that risks determined in one situation can be applied in others (ICRP 1991, 2007). The International Commission on Radiological Protection (ICRP) has developed and formalised this methodology, and define the quantities of equivalent and effective dose, which are in general use in the field. However, although these quantities are intended for use in the ICRP system of protection, in practice they are far more widely used and applied. In many circumstances, this extension of application is justifiable, whereas in others the application of ICRP methodology may be, in part or totally, inappropriate.

In general, doses resulting from external exposures are more readily assessed than those from radionuclides incorporated into the body. In addition, most information on risks to human health comes from studies on populations exposed to external radiation, while quantitative estimates of the radiotoxicity of internal emitters in humans is limited to a few radionuclides (UNSCEAR 2000, WHO 2001, ICRP 2007). For the assessment of doses from internal emitters, ICRP has developed biokinetic and dosimetric models that enable the calculation of organ and tissue doses for a wide range of radionuclides. These are used to calculate equivalent and effective dose coefficients (dose per Bq intake), considering occupational and environmental exposures (ICRP 1979, 1991, 1994a, 1996). Dose coefficients have also been given for a range of radiopharmaceuticals used in diagnostic medicine (ICRP 1987).
In response to concerns about the methods used to estimate doses and risks from internal emitters, the UK Government set up the Committee Examining Radiation Risks from Internal Emitters in 2001. The scientific and technical discussions of CERRIE, and the Final Report (CERRIE 2004) centred round three issues: dose assessment and risk (largely related to ICRP methodology), biological evidence, and epidemiological studies. The overall CERRIE (2004) view was that, for the purposes of radiological protection, the concept of combining radiation doses from internal and external emitters (with appropriate scaling and weighting) was justifiable and achievable. However, the Committee was divided on the adequacy of the methods used (by ICRP) to achieve this end and the adequacy of the methods for assessing risk. With two members dissenting, it was finally agreed that the ICRP dose assessment methodology for internal emitters was appropriate for its intended use in radiation protection. Two conclusions were that ICRP should clarify and elaborate its advice on the use of its dose quantities, equivalent and effective dose, and also that more attention should be paid to uncertainties in dose and risk estimates and their implications. The Committee on Medical Aspects of Radiation in the Environment (COMARE 2004) endorsed these recommendations in its advice to Government on the implications of the CERRIE (2004) report.

Updated ICRP recommendations have now been published (ICRP 2007) and include detailed discussions of the calculation of equivalent and effective dose and their application, with some reference to uncertainties. Increasing attention is being paid to uncertainties by Regulators and others responsible for dose assessments, as exemplified by the work of the UK National Dose Assessment Working Group (NDWG 2008).

The present paper is based on material prepared for CERRIE, updated to reflect recent developments including the ICRP 2007 recommendations. We begin with an outline of the ICRP dose assessment methodology for radionuclide intakes by ingestion or inhalation and critical commentary on its scientific basis and limitations. We follow with a discussion of sources of uncertainty in the estimation of dose and risks from internal emitters.

2. ICRP dose estimates for radionuclide ingestion or inhalation

2.1. Dose coefficients


- The use of biokinetic models to represent the distribution and retention of radionuclides in body organs and tissues, and hence to calculate the total number of disintegrations occurring in each ‘source region’.
- The use of dosimetric models to calculate mean absorbed dose, \( D_T \), to each target organ or tissue from the disintegrations and emission energies occurring in each source region. The SI unit for absorbed dose is J kg⁻¹ and its special name is gray (Gy).
- The use of radiation weighting factors, \( w_R \), to take account of the relative effectiveness of different radiation types in causing cancer and hereditary effects at low doses and dose rates, converting absorbed dose (Gy) to equivalent dose in sievert (Sv). The equivalent dose, \( H_{T,R} \), in tissue or organ \( T \) due to radiation \( R \), is given by

\[
H_{T,R} = w_R D_{T,R}
\]

and the total equivalent dose to an organ or tissue, \( H_T \), is the sum of \( H_{T,R} \) over all radiation
The use of tissues weighting factors, \( w_T \), to take account of the contribution of individual organs and tissues to overall detriment from cancer and hereditary effects, combining equivalent doses to organs and tissues to give effective dose (Sv):

\[
E = \sum_T w_T H_T
\]

where \( H_T \) is the equivalent dose in tissue or organ, \( T \), and \( w_T \) is the weighting factor for that tissue \( T \).

It should be noted that the tissue weighting factors, \( w_T \), are relative fractional quantities, derived subjectively and being based on the risk of perceived detriment, from cancers and hereditary defects, arising from the effects of radiation in each tissue type. Thus, the sum of all tissue weighting factors over the whole body is unity:

\[
\sum_T w_T = 1.
\]

While the definition of absorbed dose has the scientific rigour required of a basic physical quantity, the same is not true of the ICRP protection quantities, equivalent and effective dose, which are SI derived units. The ICRP quantities are intended for practical application in radiological protection and the choice of radiation and tissue weighting factors used in their calculation involves simplifying assumptions which the ICRP regard as acceptable for this purpose. While doses quoted in Sv are generally taken to be effective dose if this is not specified, the use of the same special name for equivalent and effective dose can lead to confusion.

The use of effective dose allows the summation of doses from different radionuclides and from external sources for comparison with dose limits and constraints set on the basis of risk relating to whole-body radiation exposure. Equivalent and effective doses are commonly integrated over a 50 year period for adults and to age 70 years for children and the resulting values are referred to as committed doses. The steps in the calculation of equivalent and effective dose are examined in more detail in the following sections.
2.2. Biokinetic models

ICRP biokinetic models consider intakes by ingestion and inhalation by adults and children (ICRP 1979, 1980, 1981, 1989, 1993, 1994b, 1995a, 1995b). Doses to the foetus following maternal intakes have also been calculated (ICRP 2001) and also doses to infants from radionuclides transferred to breast-milk (ICRP 2004). Models of the alimentary and respiratory tracts are used to define the movement of radionuclides within these systems, resulting in absorption to blood and/or loss from the body (ICRP 1979, 1994b, 2006). The behaviour of radionuclides absorbed to blood is described by element-specific systemic models (ICRP 1979, 1980, 1981, 1989, 1993, 1995a, 1995b).

Movement of ingested radionuclides through the gastrointestinal tract is quantified by transit times between the stomach, small intestine and regions of the large intestine, with absorption to blood occurring mainly in the small intestine. The proportion assumed to be absorbed to blood depends on the chemical properties of the element and, in some cases, on the chemical form ingested. The proportion may range from complete absorption, for example, for iodine or caesium, to less than 0.1%, for example, for plutonium (ICRP 1989). In the case of plutonium, several absorption factors may be used, depending on the solubility of the compounds in question. A new model of the alimentary tract has been published (ICRP 2006) in which an important development is the explicit calculation of doses to target regions in the epithelial lining of alimentary tract regions (see section 2.3).

Inhaled particles containing radionuclides are assumed to deposit in the nose, the bronchial and bronchiolar airways of the lung and the alveolar respiratory region, with deposition in the different regions being dependent on particle size (ICRP 1994a, 2002b). Removal from the lungs occurs mainly by dissolution and absorption to blood and the competing process of escalation of particles from the lung to the throat followed by their entry into the alimentary tract. The proportions absorbed to blood or escalated depend on the solubility of the material and on the radioactive half-life of the radionuclide. The ICRP model for the respiratory tract is also applicable to vapours and to inhalation of radon and its radioactive progeny.

The systemic models used to describe the behaviour of radionuclides absorbed to blood (ICRP 1979, 1980, 1981, 1989, 1993, 1995a, 1995b) range in complexity from very simple models that assume uniform whole-body distribution (e.g. hydrogen, caesium) to multi-compartment recycling models that take account of movement within and between body organs and tissues (e.g. strontium, lead, uranium, plutonium). For the simple example of hydrogen (radioisotope: tritium, $^3$H), intakes as tritiated water (HTO) or organically-bound tritium (OBT) are considered by ICRP (1989), with uniform whole-body retention of components representing HTO and OBT (half-times of retention of 10 d and 40 d, respectively; in adults; shorter in children). The most complex models are those developed for the bone-seeking alkaline earth and actinide elements (inc. strontium, radium, thorium, plutonium). These models represent the behaviour of the elements within bone, taking account of initial deposition on bone surfaces, exchange with or burial within bone mineral and movement to bone marrow (ICRP 1989, 1993, 1995a, 1995b). The physiological realism of these models includes movement between organs and tissues via the circulation. In addition, the recycling models were designed to fit excretion data and can be used for bioassay interpretation. Simpler models for other elements are less suitable for this purpose.

The reliability of biokinetic models depends ultimately on the quality of the data on which they are based, including the availability of human data, but also on the realism of the model developed from these data (see section 3, uncertainties). For a number of elements and their radioisotopes, there are few or no human data for use in model development or validation, and reliance is placed on the results of animal experiments and chemical analogues. There are
continuing efforts to provide improved models and over the next few years the ICRP’s intention will be to publish new and updated models, and dose coefficients calculated using these models, to follow the new recommendations (ICRP 2007).

We emphasise that ICRP biokinetic models are developed primarily for the calculation of dose coefficients (equivalent and effective dose per Bq intake) for use within the ICRP framework of radiological protection. However, the models are also used for other purposes, including the estimation of absorbed organ and tissue doses in epidemiological studies (e.g., Shagina et al 2007, Leggett et al 2005) and medical applications. In such applications, it is important that the applicability of models to the specific circumstances of exposure is carefully considered. Thus, for example, for the calculation of plutonium-239 doses to workers at the Russian Mayak plant, a modification of the ICRP biokinetic model was developed (Leggett et al 2005).

The essential precursor to the use of the ICRP models is, of course, the quantification of intakes. For occupational intakes, the ICRP biokinetic models may be used to assess doses on the basis of bioassay measurements of, for example, whole-body retention or urinary excretion. Intakes may also be estimated by measuring radionuclide concentrations in the working environment (specifically, air concentrations). For environmental exposures, estimates of intakes are based on measurements of radionuclides in diet and air, and may involve the use of food-chain models. In many cases, a major contributor to uncertainties in dose estimates will be uncertainties on intakes.

2.3. Dosimetric models

Biokinetic models for individual elements and their radioisotopes are used to calculate the total number of radioactive decays (transformations) occurring within specific tissues, organs or body regions (source regions) during a given period of time (usually to age 70 y). Dosimetric models are used to calculate the deposition of energy in all important organs/tissues (targets) for transformations occurring in each source region, taking account of the energies and yields of all emissions (Eckerman 1994). Absorbed dose in gray can then be calculated, knowing the number of decays occurring in source regions and energy deposition in target regions.

Dose calculations involve the use of nuclear decay data (Eckerman et al 1994, Endo et al 2003, 2004) and anthropomorphic phantoms that describe geometric relationship between different tissues and organs. There are two main types of phantom—mathematical phantoms that approximate the sizes and shapes of organs mathematically (Cristy and Eckerman 1987) and voxel phantoms that use tomographic data for real individuals obtained using computed tomography or magnetic resonance imaging (Zankl et al 2002, 2003, 2007). ICRP currently uses mathematical phantoms that have been developed for adults and children of different ages (Eckerman 1994), and for the pregnant woman and foetus for each trimester of pregnancy (Stabin et al 1999, ICRP 2001). Voxel phantoms for a reference adult male and female are currently being developed for use by ICRP (Zankl et al 2003, 2007, Fill et al 2004), adjusting data from scanned images for consistency with ICRP reference data for the body mass and related characteristics of adult males and females (ICRP 2002c). New reference computational phantoms will also be developed for children of different ages for use in the calculation of dose coefficients for members of the public (ICRP 2007).

Doses from ‘cross-fire’ radiation between source and target tissues are important for penetrating photon radiation. For ‘non-penetrating’ alpha and beta particle radiations, energy will in most cases be largely deposited in the tissue in which the radionuclide is deposited. However, source and target considerations are taken into account for alpha and electron emissions in a number of important cases. These include:
- doses to target cells in the walls of the bronchiolar airways from radionuclides in the mucus layer within the airway (ICRP 1994b);
- doses to target regions in the gut from radionuclides in the lumen, particularly in the new ICRP (2006) model of the alimentary tract (Harrison et al 2005, Phipps et al 2007);
- doses to cells adjacent to inner bone surfaces (taken currently to be a 10 µm layer) and all red marrow from radionuclides on bone surfaces and within bone mineral (ICRP 1979);
- cross-fire irradiation between foetal tissues for electron emissions (ICRP 2001).

For all dose calculations, radionuclides are assumed to be uniformly distributed throughout source regions, although these can be whole organs (e.g. liver) or a thin layer within a tissue (e.g. bone surfaces). Similarly, target cells are assumed to be uniformly distributed throughout target regions that vary in size from whole organs to layers of cells. An important concern is whether these assumptions provide adequate assessments of dose and risk, particularly when considering the heterogeneous distribution of short-range charged particle emissions (e.g. alpha emitters, low energy beta emitters such as tritium, and Auger emitters) in relation to target cells and their nuclei (see section 3).

In addition to their use for ICRP dosimetry in the calculation of dose coefficients for internal emitters and conversion coefficients for external radiation, the new generation of voxel phantoms will be better suited for other applications. Thus, adjustments can be made to the body shape and organ dimensions of specific individuals so that they can be used, for example, for medical applications in which accurate estimates of absorbed doses are required.

2.4. Relative biological effectiveness, \( w_R \) and equivalent dose

The next stage in the ICRP methodology, the calculation of equivalent dose, provides a method by which the individual radiation doses to a given tissue or organ, from various types of ionising radiation (alpha, beta, gamma and x-rays), can be summed in relation to the effect they produce and, specifically, in relation to their cancer-producing effects. To achieve this objective, major simplifications are made.

Different types of radiation are known to vary in their effectiveness in causing cancer (ICRP 1991, 2003, 2007, UNSCEAR 2000). These differences can be related in principle to the three-dimensional structure of ionisation tracks produced by charged particles traversing tissue volumes of interest, containing sensitive cellular targets including chromosomal DNA. The linking of biological effects to track structure is one of the central research goals in the field of microdosimetry. Currently, a simple one-dimensional indicator of track structure, namely the linear energy transfer or LET, is used to inform judgments on biological effects (ICRP 1991, 2003, UNSCEAR 2000). Clustered DNA damage, together with the degree of complexity of the damage, has been shown to increase with LET (Nikjoo et al 2002, ICRP 2003). The ultimate biological consequence is dependent on whether the damage can be repaired and with what fidelity. Types of clustered damage may compromise DNA repair fidelity and can lead to an increase in mutation frequency (Gulston et al 2004, Pearson et al 2004). The two broad categories of radiation that require consideration in the context of internal dosimetry are photons and charged particles, the latter including electrons and alpha particles. In microdosimetric terms, the rate of energy deposition per unit length of the track of a given charged particle depends on the particle’s momentum, energy and velocity. Alpha particles (high energy, relatively large mass and momentum, low velocity) have relatively high LET values, whilst electrons (generally lower energy than alpha particles but far lower mass and therefore greater velocity) have, in general, relatively lower LET values. However, for a given particle, as its velocity decreases the density of ionisation along its track increases, giving rise to a pronounced peak in ionisation density towards the end of its track—the so-called Bragg Peak.
In consequence, whilst the LET value of moderate and high energy electrons is relatively low over most of the track structure, LET is higher at track ends and, given the branching structure of electron tracks, this leads to a disproportionate importance of track ends in the biological effectiveness of beta particles. Additionally, very low energy electrons (e.g. Auger electrons, beta emission from $^3$H, electrons released by absorption of low energy x-rays) have higher LET values than higher energy beta particle emissions or electrons generated by conversion of gamma photons.

Relative biological effectiveness (RBE) is defined as the ratio of the absorbed dose of a reference radiation to the absorbed dose of a test radiation which is required to produce the same level of biological response in a particular animal or in vitro cellular study (ICRU 1986, ICRP 2003). RBE is therefore an empirical quantity, which depends on the biological system and the conditions of the experiment. It is usually found to vary with dose and dose rate, increasing for high LET radiation to a maximum value at low dose and dose rate because of a curvilinear response at higher acute doses of the reference low LET radiation. RBE_{MAX} values are applicable to estimation of stochastic risk at low doses (UNSCEAR 2000, ICRP 2003, 2007).

The limited human data that allow comment on alpha particle RBE values are referred to below (section 2.5). They are consistent with values of RBE compared to low LET radiations of around 20 for lung and liver cancer and lower values for bone cancer and leukaemia, although considerable uncertainty must attach to any numerical estimate of RBE from these data (Harrison and Muirhead 2003). However, there is good evidence from animal and in vitro studies of RBE values for alpha emitters of around 10 or greater for some cancer-related effects, and low values of 1–2 for leukaemia (WHO 2001, ICRP 2003). Human and animal data for bone cancer induction by alpha-emitting radionuclides suggest that there may be a threshold dose for some cancer types (UNSCEAR 2000, Harrison and Muirhead 2003).

Low LET radiations show differences in RBE that generally reflect differences in their average ionisation density (HPA 2007). Thus, for example, low energy beta emissions from tritium ($^3$H) decay have been shown to have RBE values of up to between 2 and 3 (compared to gamma rays), for in vitro end-points including cell killing, mutation and induction of chromosomal aberrations (Straume and Carsten 1993, Straume 1993, Harrison et al 2002, Fairlie 2007, HPA 2007, Bridges 2008). For photons, an increase in RBE with decreasing energy is supported by theoretical calculations (Nikjoo and Goodhead 1991) and experimental observations (Hill 2004). Thus, compared to $^{60}$Co gamma rays, 29 kVp mammography x-rays have higher RBE values than 220 kVp x-rays by up to a factor of 4. Such RBE values have been observed for dicentric chromosome aberrations and cell transformation with mammalian cells in vitro and are likely to be smaller in larger tissue masses (ICRP 2007).

In the calculation of equivalent dose (see section 2.1), the ICRP uses broad judgments to smooth over observed differences in RBE by the use of generic radiation weighting factors ($w_R$). For convenience, ICRP class electrons (beta particles) and photons (x- and gamma radiation, both of which are absorbed to give ionising electrons) as low LET radiations, and alpha particles as high. The $w_R$ values of most relevance to internal emitters are then set to 20 for alpha particle irradiation, and 1 for all low LET radiations (ICRP 1991, 2007). In a rigorous scientific sense, this procedure would not be regarded as acceptable. However, as a procedure in radiological protection, this approach is defended on the grounds of simplicity, practicality and transparency (see section 2.6). On this subject, the CERRIE (2004) report says: ‘...if the purpose of the dose estimation is for comparison with regulatory limits, and use of generic radiation weighting factors leads to estimated effective doses well below the need for intervention, it can be accepted that using scientifically more rigorous (and probably costly) calculation methods would not have affected the outcome.’ We accept that increased
complexity in radiation weighting may not improve protection and could over-interpret current knowledge. However, we consider it important that uncertainties in the effectiveness of different radiation types in causing cancer at low doses are included in overall estimates of uncertainties when assessing the adequacy of protection and considering optimisation (see sections 2.6 and 3).

2.5. Risk estimates, $w_t$ and effective dose

The purpose of the final stage in the ICRP methodology is to relate dose to risk in a simple manner, amalgamating all radiation doses, however received, into one quantity, the effective dose, which has a direct relationship with overall risk. In so doing, all separate information with respect to risks of cancers to specific organs is lost; effective dose is a whole-body quantity defined for a reference person. ICRP’s intention is that an estimated effective dose is a quantity to be used for testing compliance with dose limits and constraints, and is not intended for the calculation of doses to specific individuals, for whatever purpose. For estimation of radiation doses to individuals, or the risk to similarly-exposed groups of individuals of contracting a specific cancer, the last step in the ICRP model is entirely inappropriate (see section 2.6).

Risk estimates for radiation-induced cancers are largely derived from studies of the effects of external radiation, the principal source of information being long-term studies of those who survived the immediate effects of the atomic weapons’ explosions at Hiroshima and Nagasaki, in 1945 (the so-called A-bomb survivors). Thus, the risk of developing or dying from each observed type of cancer has been related to the estimated external radiation dose received at the time of the explosion, and for a short time thereafter from gamma radiation from environmentally deposited radionuclides. Doses from inhaled or ingested radionuclides were not assessed. The cancer incidence and mortality data for A-bomb survivors show a statistically significant increase in solid cancers at doses from around 100 mGy up to around 3 Gy (UNSCEAR 2000, Preston et al 2003, 2007). The data on solid cancer incidence indicate that any dose threshold (i.e. below which risks are not increased) would not exceed 85 mGy (Preston et al 2007). Separate studies of cancers in children exposed in utero to x-rays during diagnostic radiography, principally the Oxford Survey of Childhood Cancers (OSCC), have shown statistically significant increases in childhood leukaemia and solid cancers at doses of the order of 10 mGy (Bithell and Stewart 1975, Wakeford and Little 2003). The risk per unit dose estimated for the OSCC was compatible with that obtained from the A-bomb survivor studies, although there are large uncertainties (Wakeford and Little 2003). In applying the risk estimates derived from the A-bomb survivor data to cancer risks at low doses and dose rates, ICRP apply an empirical correction factor, the Dose and Dose Rate Effectiveness Factor (DDREF), assuming a value of two for solid cancers (ICRP 1991, 2007). This assumption that risks per unit dose are lower at lower doses and doses rates is based largely on animal and in vitro data showing curvilinear dose-response relationships for exposure to acute low LET radiation. No DDREF is applied when considering risks from high LET radiation. The BEIR VII committee (NAS/NRC 2006) recently undertook probabilistic analyses of dose-response data and obtained a modal value for DDREF of 1.5. However, judgments on an appropriate value for DDREF depend on the weight given to different sources of data. On the basis of the A-bomb survivor data, it is not possible to distinguish between a DDREF of 1 (no DDREF) or 2 for solid cancers (UNSCEAR 2000, Preston et al 2003). Experimental data generally show greater values and the ICRP (2007) judgment is that a value of 2 should continue to be applied. For leukaemia, the A-bomb survivor data are consistent with the use of a linear-quadratic dose–response relationship and DDREF is not applied.
Having obtained risk estimates for exposures at low doses of a few tens of mGy and below, ICRP assume a linear relationship between dose and risk. It is the consensus view that this ‘linear non-threshold’ assumption (LNT) is the best approach on current evidence for radiation protection purposes (Preston 2003, NCRP 2001, ICRP 2006, 2007). Indeed, the LNT assumption is essential for the operation of the current protection system, allowing the addition of external and internal doses of different magnitudes, with different temporal and spatial patterns of delivery. Nevertheless, the LNT dose-response remains controversial, with arguments for supra-linear low dose responses and for thresholds and/or hormetic effects (CERRIE 2004, French Academy of Science 2005, Tubiana et al 2008, Feinendegen et al 2008). ICRP (2007) conclude that the true validity of the LNT model may prove to be beyond definitive resolution for the foreseeable future. For reasons of practicality, it is highly desirable to retain the LNT assumption unless or until this position becomes scientifically untenable.

A central concern of CERRIE (2004) was whether the risk factors derived from studies of the A-bomb survivors can be applied generally. These risk factors, which applied to short, homogeneous, high external doses of gamma radiation at a high dose rate, are applied in all situations, including those at the opposite extreme in almost all respects: namely heterogeneous, low dose exposures to charged particles at low dose rates over protracted time periods. Although CERRIE concluded that these risk factors were the best available, the Committee expressed considerable reservations and considered that the application of these factors constituted an important source of uncertainty in dose and risk estimates.

In relation to the application of external risk factors to internal exposure to alpha particle irradiation, a number of human studies (UNSCEAR 2000, WHO 2001) provide information that has been used by ICRP (1991) and others to estimate risks of liver, bone and lung cancer:

- Liver cancer—patients given intravascular injections of ‘Thorotrast’, a colloidal thorium oxide preparation (232Th, an alpha emitter), as a contrast medium for diagnostic radiology.
- Bone cancer—occupational exposure of radium dial painters to 226Ra and 228Ra; patients given 224Ra for medical conditions.
- Lung cancer—occupational exposure of uranium miners to radon-222 and daughters, with consistent data from studies of residential exposure.

In addition, an excess of leukaemia has been reported in Thorotrast-treated patients, and quantitative estimates of 239Pu induced lung cancer have been derived for Russian workers at the Mayak nuclear site (WHO 2001, Harrison and Muirhead 2003, Gilbert et al 2004). Comparisons can be made between the risk estimates for radiation-induced cancer derived for these radionuclide exposures, and those derived for the atomic bomb survivors (Harrison and Muirhead 2003). On the assumption of an alpha RBE of 20, the incidence of liver cancer in Thorotrast patients is consistent with that in the A-bomb survivors. However, comparison of leukaemia incidence in the two population groups can only be made consistent by reducing the applied 232Th alpha RBE to around 1–2. This suggests that alpha irradiation of bone marrow is less effective in causing leukaemia than would be predicted on the basis of standard ICRP assumptions. Animal data provide some support for a low alpha RBE for leukaemia induction (Breckon and Cox 1990, Ellender et al 2001). Estimates of lung cancer risk in miners exposed to 222Rn and its short-lived alpha-emitting progeny, obtained using the ICRP respiratory tract model and an alpha particle RBE of 20, are within a factor of about 3 of estimates based of the A-bomb survivor data (Harrison and Muirhead 2003). Similar approximate risk estimates have been derived for 239Pu induced lung cancer in Mayak workers (Grogan et al 2001, Gilbert et al 2004), although there are large uncertainties in estimates of lung dose. Recent combined case-control analyses have provided information on raised rates of lung cancer attributable to exposures to 222Rn and its progeny in homes (Darby et al 2005, 2006, Krewski et al 2006,
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Lubin et al. 2004). Precise comparisons with risk estimates derived from the miner data and the A-bomb survivor data are difficult but they appear to be broadly consistent (ICRP 2007).

Overall, the comparisons that are possible using human data show enough consistency between estimates of radiation risk from internal emitters and external radiation for the two to be combined. Support is also provided by animal and in vitro data comparing the effects of different radionuclides and external radiation (UNSCEAR 2000, WHO 2001). However, uncertainties in the dose estimates for internal emitters and in the risk factors mean that overall the uncertainty in any estimate will be considerable, and possibly significant (Harrison and Muirhead 2003, ICRP 2007). Uncertainties are discussed in more detail later.

In the calculation of effective dose (see section 2.1), the ICRP (1991, 2007) uses a single set of tissue weighting factors \( w_T \) to express the contribution of individual organs and tissues to overall detriment from cancer and hereditary effects, relating to whole-body radiation exposure. Table 1 shows the values introduced in the new ICRP (2007) recommendations and the Publication 60 (ICRP 1991) values. The main source of data on cancer risks was the follow-up studies of the Japanese atomic bomb survivors, used to derive risk coefficients averaged over seven western and Asian populations with different background cancer rates (ICRP 2007). The new \( w_T \) values are based on cancer incidence rather than fatality data, adjusted for lethality, loss of quality of life and years of life lost. Weighting for hereditary effects is now based on estimates of disease in the first two generations rather than at theoretical equilibrium. The main changes in \( w_T \) values in the new recommendations are an increase for breast (from 0.05 to

### Table 1. ICRP tissue weighting factors, \( w_T \), and relative detriment values for all ages at exposure (0–85 y).

<table>
<thead>
<tr>
<th>Organ/tissue</th>
<th>( w_T ) ICRP (1991)</th>
<th>( w_T ) ICRP (2007)</th>
<th>Sex-averaged</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>0.05</td>
<td>0.12</td>
<td>0.139</td>
<td>0.000</td>
<td>0.240</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>0.12</td>
<td>0.12</td>
<td>0.107</td>
<td>0.144</td>
<td>0.080</td>
</tr>
<tr>
<td>Colon</td>
<td>0.12</td>
<td>0.12</td>
<td>0.083</td>
<td>0.138</td>
<td>0.044</td>
</tr>
<tr>
<td>Lung</td>
<td>0.12</td>
<td>0.12</td>
<td>0.157</td>
<td>0.124</td>
<td>0.182</td>
</tr>
<tr>
<td>Remainder</td>
<td>0.05</td>
<td>0.12</td>
<td>0.198</td>
<td>0.256</td>
<td>0.155</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.12</td>
<td>0.12</td>
<td>0.118</td>
<td>0.120</td>
<td>0.117</td>
</tr>
<tr>
<td>Gonads</td>
<td>0.20</td>
<td>0.08</td>
<td>0.061</td>
<td>0.053</td>
<td>0.068b</td>
</tr>
<tr>
<td>Bladder</td>
<td>0.05</td>
<td>0.04</td>
<td>0.029</td>
<td>0.036</td>
<td>0.242</td>
</tr>
<tr>
<td>Liver</td>
<td>0.05</td>
<td>0.04</td>
<td>0.046</td>
<td>0.075</td>
<td>0.026</td>
</tr>
<tr>
<td>Oesophagus</td>
<td>0.05</td>
<td>0.04</td>
<td>0.023</td>
<td>0.026</td>
<td>0.021</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.05</td>
<td>0.04c</td>
<td>0.022</td>
<td>0.010</td>
<td>0.031</td>
</tr>
<tr>
<td>Bone surfaces</td>
<td>0.01</td>
<td>0.01</td>
<td>0.009</td>
<td>0.011</td>
<td>0.008</td>
</tr>
<tr>
<td>Brain(^d)</td>
<td>—</td>
<td>0.01</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Salivary glands(^d)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Skin</td>
<td>0.01</td>
<td>0.01</td>
<td>0.007</td>
<td>0.008</td>
<td>0.006</td>
</tr>
</tbody>
</table>

\(^a\) The ICRP (2007) weighting factor of 0.12 for remainder is apportioned equally between 13 organs/tissues in males and females: adrenals, extrathoracic tissue, gall bladder, heart, kidneys, lymphatic nodes, muscle, oral mucosa, pancreas, prostate (♂), small intestine, spleen, thymus, uterus/cervix (♀).

\(^b\) Combined detriment from ovarian cancer and hereditary effects.

\(^c\) The weighting factor for the thyroid was set at 0.04 to take account of evidence of a pronounced elevation of risk in childhood.

\(^d\) Salivary glands and brain were given weighting factors of 0.01 because cancer risks, while not separately quantifiable, were judged to be greater than for other tissues in the remainder.
0.12), a decrease for gonads (from 0.2 to 0.08) and inclusion of more organs and tissues in a larger 'Remainder' (from 0.05 to 0.12). The sum of $w_T$ over all tissues (a vertical column if table 1) is equal to 1. Two points need to be emphasised. Firstly, in calculating effective dose, it is essential that the contribution from all organs/tissues specified in table 1 be included. Secondly, because the effective dose is calculated by summing the product ($w_T \times$ equivalent dose) for each organ or tissue, the risks of cancer or other detriment in these tissues individually has been lost. If the purpose of the dose estimation was to assess the risk of a specific cancer, then calculation of effective dose is inappropriate—equivalent dose to the specific tissue should be used instead.

Annex A of the new ICRP (2007) recommendations provides a detailed explanation of the calculation of $w_T$ values, including a summary of the steps involved (p 191). Tables are given of age- and sex-averaged risk coefficients and absolute and relative detriment values, comparing different methods of calculation. Tables are also given summarising sex-specific, age-averaged values calculated as an intermediate stage. The age- and sex-averaged relative detriment values for all ages (0–85 y) are shown in table 1, together with the corresponding sex-specific values. There are substantial differences between males and females in relative detriment values for some organs (colon, liver, thyroid) and breast cancer is estimated to account for about one-quarter of the total detriment in females (ICRP 2007). The estimates provided by ICRP (2007) also show absolute detriment in females to be 40% greater than in males. ICRP (2007) has not published age-specific risk estimates. BEIR VII (NAS/NRC 2006) gave estimates for a US population of life-time attributable risk for radiation exposure of males and females at different ages. In general, risk estimates were about double for irradiation in infancy compared with age 20 y, and about 5–6 times greater for thyroid cancer.

2.6. Application of ICRP protection quantities

Sections 2.2–2.5 of this review have provided some details of the steps involved in the calculation of ICRP dose coefficients for the ingestion and inhalation of radionuclides. These are values of committed equivalent dose and committed effective dose per Bq intake (see section 2.1); that is, doses integrated over a 50 year period for adults and to age 70 years for children. The ICRP protection quantities, equivalent and effective dose were devised for use within the ICRP system of protection, to enable the summation of doses from different radionuclides and from external sources for comparison with dose limits and constraints. Doses are calculated using defined biokinetic and dosimetric models, including reference anatomical data for the organs and tissues of the human body. They are calculated for reference adults, children of different ages and the foetus at different stages of development. They do not take account of individual characteristics. Radiation weighting factors allow for the greater effectiveness of alpha particles than low LET radiations, per unit absorbed dose, in causing stochastic effects at low doses and dose rates. However, they do not attempt to address the complexity of, for example, observed differences between low LET radiations (e.g. photons and electrons of different energies) and of different alpha particle RBE values for different cancer types. Tissue weighting factors are used to take account of the contribution of individual organs and tissues to overall detriment from cancer and hereditary effects, providing a simple set of values based on a series of complex judgments. They are rounded values chosen on the basis of age- and sex-averaged values of relative detriment, calculated from risk coefficients applying as averages over a number of populations with different background cancer rates. Following the publication of new ICRP (2007) recommendations, revised dose coefficients will be published over the next few years, first for workers, then for members of the public. With the introduction of reference computational phantoms, doses will be calculated separately for
males and females and equivalent doses will be averaged for the calculation of effective dose (figure 2).

There is an apparent inconsistency of approach between that taken to the development of biokinetic and dosimetric models and that taken to the choice of radiation and tissue weighting factors. The models continue to increase in complexity as more experimental data becomes available and their physiological realism is improved, whereas the weighting factors remain as simplified representations of the underlying science. However, while the biokinetic and dosimetric models are primarily intended for use in the calculation of ICRP dose coefficients, they can be more widely applied. For example, they can be and are used to calculate absorbed doses to specific organs and tissues, both in the assessment of risks of stochastic effects and in the assessment of deterministic effects at higher doses. The models can also be used to provide dose estimates for epidemiological studies and in probability of causation calculations. The new generation of computational phantoms is ideally suited for these other applications. Thus, adjustments can be made to the body shape and organ dimensions of specific individuals so that they can be used, for example, for medical applications in which accurate estimates of absorbed doses are required. In contrast, radiation and tissue weighting factors are to be used solely in the calculation of the ICRP protection quantities, to provide a method for comparing all radiation exposures with dose limits and constraints. It would not be practicable to devise

Figure 2. Sex-averaging in the calculation of effective dose to adults.
an internationally applicable system that would take account of recognised age-, sex- and population-related differences in risk factors, and to attempt to do so would introduce unhelpful complexity that would almost certainly not improve protection. Similar considerations apply to a more complex treatment of radiation weighting and there is also a possibility that an increase in complexity would create a false impression of the certainty with which radiation risks at low doses are understood. Central to the ICRP system is the optimisation of protection below constraints (ICRP 2007); constrained optimisation should ensure appropriate levels of protection, using the protection quantities with their inherent and unavoidable simplifications.

Committed effective dose can be seen to provide a convenient whole-body parameter for comparison with dose limits, constraints and optimised levels. However, use of effective dose does not reveal any information about the way in which the dose is made up, and indeed can conceal very different contributions to dose and risk from the irradiation of individual organs or tissues, and in the time-course of dose delivery. For example, consider groups of individuals each exposed to a committed effective dose of 10 mSv. The doses to each group may comprise an almost infinite variety of components a group might have received. Examples, calculated using Publication 60 (ICRP 1991) weighting factors, are:

(a) a uniform whole-body dose of 10 mGy from external low LET radiation;
(b) a committed equivalent dose of around 200 mSv (200 mGy) to the thyroid (with very low doses to other tissues) after ingestion of iodine-131 (thyroid \( w_T = 0.05 \)); and,
(c) committed equivalent doses largely to liver (~70 mSv) and skeletal tissues (bone surface ~340 mSv; red bone marrow ~15 mSv) after ingestion of \(^{239}\)Pu (absorbed doses of ~4 mGy to liver, 17 mGy to bone surfaces and 1 mGy to red bone marrow).

While the overall detriment (effective dose) would be deemed to be the same in each case, the distribution of risk between cancer types would be very different. In addition, the time-course of dose delivery can vary widely. While both the external dose and the internal dose from \(^{131}\)I would be delivered within the year following intake, the dose from \(^{239}\)Pu, because of its long half-life and long retention times in tissues, would be delivered over 50 years, with only about 5% in the first year.

The ICRP recommendations (ICRP 1991, 2007) have included discussion of the intended purpose of the protection quantities, for the regulatory control of radiation exposures. ICRP (1991) states that: ‘for the estimation of the likely consequences of an exposure of a known population, it will sometimes be better to use absorbed dose and specific data relating to the relative biological effectiveness of the radiations concerned and the probability coefficients relating to the exposed population’. This issue is addressed in more detail in the new recommendations (ICRP 2007), and by Harrison and Streffer (2007). It is clear that equivalent and effective dose are not intended for use in assessments of deterministic effects, in assessing cancer risks in epidemiological studies, in probability of cancer causation calculations, or any other situation where best estimates of doses and risks to specific individuals or groups are being considered. In such cases where the use of ICRP methodology is not appropriate, mean absorbed doses in organs and tissues are measured in Gy and estimates of uncertainties will also, in general, be appropriate. Equivalent and effective dose are often inappropriately used. It is also unfortunately the case that when reference is made simply to dose in Sv, although this will generally be committed effective dose, it may also be committed equivalent dose to a specific organ or tissue, or even absorbed dose to tissues, which should always be expressed in Gy. Strictly, the term dose should be reserved for the scientific quantity, absorbed dose (Gy), and reference to the protection quantities should always distinguish between committed equivalent dose and committed effective dose.
3. Uncertainties in doses and risks from internal emitters

3.1. Uncertainty in relation to intended application

Uncertainties are associated with all aspects of the estimation of doses and risks at low doses. Uncertainties in biokinetic models and their parameter values depend on the availability of reliable data and often include the applicability of animal data to humans. Dosimetric uncertainties include the treatment of source and target distributions within tissues for radionuclides with short-range emissions. RBE values are often difficult to assess from available animal and human data and the applicability of in vitro end-points to cancer in humans may be questionable. Uncertainties in estimates of cancer risks relate to assumptions regarding the transfer of risks across populations, the validity of different risk models, the use of a dose and dose rate effectiveness factor (DDREF) and the use of a linear dose-response relationship at low doses. Assessments of uncertainties in risk estimates and in radionuclide doses have been published but there is as yet no comprehensive information on uncertainties for a range of radionuclides (CERRIE 2004). The importance of considering uncertainties where appropriate has been recognised by ICRP and others (CERRIE 2004, ICRP 2006, 2007).

Uncertainties in dose and risk estimates are clearly of variable importance depending both on the scale of the uncertainty and the purpose for which the estimates are being made. For example, the ICRP scheme for dose and risk assessment is stated to be for the specific purposes of planning and testing compliance with dose limits, constraints and reference levels (ICRP 2007, Harrison and Streffer 2007). It is held that because intervention levels and constraints are well below dose limits, and because of the requirement to optimise protection below constraints, it is unnecessary and unhelpful to attempt to include specific estimates of uncertainties in dose assessments on a routine basis. On the other hand, in epidemiological studies, uncertainty as to doses received will often be a limiting factor in the reliability of any conclusions.

The purpose of this section is to consider types and sources of uncertainty and reach conclusions on the need to consider uncertainties in different circumstances.

3.2. Types and sources of uncertainty

Uncertainties in dose and risk estimates can be categorised as numerical, mechanistic and conceptual. Numerical uncertainties refer to uncertainties in the values of physical quantities used in calculations, such as parameters for models or data for input to models. It is to be supposed that the physical quantity in question has a single value, or a central value within a definable range, which can in principle be determined. Uncertainty in a physical quantity may in general be quantified and expressed as an error, and treated by statistical methods using such measures as standard deviation, skewness, ranges between certain percentiles, etc. It should normally be possible to arrive at an at least semi-quantitative estimate—maybe as a range or order of magnitude—of uncertainty arising from numerical sources.

Mechanistic uncertainties arise largely from the use of numerical/mathematical models to represent physical systems. The use of numerical models at all levels is essential for the quantitative prediction of risk within the framework of the ICRP or any other evaluation system. The framework will consist of a number of individual sub-models, operating both in series and in parallel, and mechanistic uncertainty arises from the possibility that one or more of these models may not represent the intended biological system sufficiently well for meaningful output to be produced. It may also be that an otherwise usable model is being used outside the numerical ranges in which it is valid (this would apply, for example, in the case of a nonlinear detriment response to absorbed dose).

Conceptual uncertainties arise if the overall methodology of the assessment system, or parts of it, comes into question. Examples are the use of the linear non-threshold (LNT)
model, which allows dose summation from a multiplicity of sources, or the ‘committed dose’ assumption, which assumes that the temporal distribution of doses received by an organism can be ignored. A more fundamental example is the assumption of homogeneity of radionuclide distribution when calculating organ and tissue doses under the ICRP system, as opposed to the use of microdosimetry.

For both mechanistic and conceptual uncertainties, it is unlikely that a formal numerical treatment can be applied. Any uncertainty will usually be a guess, but this does not mean such estimates valueless, provided they are based on genuine and realistic evaluations. Even the conclusion of a committee may be of value, dependent of course on the membership of the committee. The CERRIE (2004) report summarised the committee’s conclusions with regard to uncertainty as follows: ‘Uncertainties in estimating equivalent dose, which combine the uncertainties in estimating both absorbed dose and RBE, are always likely to be significant, and probably vary in magnitude from around a factor of two or three above and below the central estimate in the most favourable cases (i.e. where good data were available) to well over a factor of ten in unfavourable ones (i.e. where they were not).’ In our view, even this rather vague statement is preferable to seemingly anodyne phrases such as ‘reasonable agreement’ or ‘probably not far in error’.

It is important to distinguish between uncertainty and variability, or more correctly, to consider variability as a component of uncertainty in certain cases. Uncertainty is generally taken to refer to the level of confidence that can be placed in given parameter values or dose estimates as central values for a population. Variability, in the limited sense of dose and risk assessment, refers to quantitative differences between different members of the population in question, and in this limited sense is biological variability.

3.3. Uncertainties in models

The reliability of biokinetic models depends both on their physiological realism and on the quality of the data on which they are based, and these two factors are, of course, interrelated. In general, a biokinetic model has two types of structural component: compartments and transfers. Compartments are related to anatomical regions, such as ‘liver’, or ‘bone surface’, and the ‘transfers’ to physiological pathways. However, the degree to which this represents physiological reality depends on the amount, reliability, and general applicability of physiological information. Adding compartments to a model may appear to increase the model’s physiological reality, and may often improve the level of ‘agreement’ with limited data simply because there are more model ‘parameters’ to adjust (in mathematical terms, the model is under-determined—there are more unknowns than there are data). However, without reliable experimental data, both to establish parameter values and, separately, to validate the model’s performance, such an apparent improvement is entirely spurious.

Uncertainties in biokinetic models also depend on the complexity of behaviour of the radionuclide that needs to be represented (Leggett et al 1998, Leggett 2001, 2003). In some cases, good human data are available, a simple model can be used and uncertainties are small (e.g. tritium as HTO in adults). In other cases, assumptions rely on animal data and/or chemical analogy between elements, and uncertainties can be substantially greater (e.g. doses to the bone marrow in children and the foetus from $^{239}$Pu). A primary source of uncertainty is the chemical form of the radionuclide inhaled or ingested (Harrison et al 2001). ICRP dose coefficients are based on generic assumptions regarding inhaled particle sizes and the solubility of radionuclides in the respiratory and alimentary tracts. Specific information may be available on the chemical form of the intake. It would be inappropriate, for example, to use the generic model for ingested caesium-137 if the intake was known to be in an insoluble particulate form.
Default assumptions regarding solubility in the respiratory tract can and should be substituted by specific information when the intake is of known chemical form (ICRP 2002b).

A further source of uncertainty in biokinetic models is the design of the models themselves and the adequacy of their representation of the physiological and biochemical processes determining the distribution and retention of radionuclides (NCRP 1998, Leggett 2001). An example might be uncertainties concerning the differences between bone-seeking, alpha-emitting radionuclides in their distribution on different bone surfaces (resting, growing, resorbing), their rates of incorporation into bone mineral, and propensity for uptake by macrophages in red bone marrow—determining the risks of bone cancer and leukaemia. A fundamental problem is that whilst physiological systems are generally highly complex, the mathematical representations of them (i.e. the models) need to be simple enough to be constructed and parameter values set on the basis of available experimental data. Ideally, independent experimental data should be available to validate the model once set up. Shortage of detailed experimental data, especially from humans, is a major factor in the uncertainties associated with biokinetic models.

Simplifying assumptions made in the calculation of dose that may not always be realistic include the homogeneous distribution of both radionuclides and deposited energy within source regions and the homogeneous distribution of target cells within target regions. Uncertainties are also introduced by the assumptions made in the formulation of mathematical phantoms. Questions arise regarding the use of dose as an indicator of harm, and hence as a measure of risk from internal emitters. This applies particularly to high LET radiation (alpha particles), but may also apply to emitters of low energy electrons (e.g. beta particles from $^3$H or Auger emitters). These concerns stem from the recognition that at low exposure levels, some cells are traversed by alpha particles (or low energy electrons), whilst many cells are not irradiated. Thus, the distribution of absorbed dose at the cellular level may be very heterogeneous.

Overall, uncertainties in dose coefficients can be regarded as small for some radionuclides (e.g. $^3$H, $^{137}$Cs, $^{131}$I) but substantially larger for other radionuclides, particularly when considering intakes by children or doses to the foetus (e.g. $^{210}$Pb, $^{210}$Po, $^{239}$Pu, $^{241}$Am). Reliable quantitative estimates of uncertainties in dose estimates for a range of radionuclides are not yet available. However, published data (Leggett et al 1998, Harrison et al 1998, Apostoaei and Miller 2004) indicate that for estimates of doses to individual tissues/ organs from some radionuclides, uncertainties may be large, with estimates of 90% confidence intervals of an order of magnitude or more above and below the central estimate. A detailed analysis of confidence intervals (97.5/2.5%) for organ dose coefficients for adults resulted in ranges of about 3–6 for $^{137}$Cs (all tissues), 7–8 for thyroid dose from $^{131}$I, and 20–40 for bone surface and red bone marrow doses from $^{90}$Sr (Apostoaei and Miller 2004). In a large exercise on uncertainties (Goossens et al 1997, Harrison et al 1998), involving aggregation of ranges obtained by a panel of experts, confidence intervals (95/5%) for adults varied from factors of less than 10 for $^{137}$Cs and for $^{131}$I thyroid dose, to factors of several thousand for $^{90}$Sr lung dose after inhalation and $^{239}$Pu bone marrow dose after ingestion. These larger ranges were partly attributable to uncertainties over the chemical forms that might be ingested or inhaled (Harrison et al 1998): the estimated uncertainty ranges differed substantially between the study experts.

3.4. Uncertainties in risk estimates

The US National Council on Radiation Protection and Measurements (NCRP 1997) have published a detailed analysis of uncertainties in risk estimates for radiation-induced fatal cancer, based on the Japanese A bomb survivor data, including uncertainties in applying risks across
populations and to low dose exposures. Their overall estimate for the 90% confidence intervals on the risk estimate show a range from a factor of 2.5–3 both below and above the 50th percentile values, corresponding to a life-time cancer risk of $1–8 \times 10^{-2}$ Sv$^{-1}$, with a mean of $4 \times 10^{-2}$ Sv$^{-1}$. Other analyses have reached similar conclusions (EPA 1999, Goossens et al 2000). Uncertainties in DDREF were estimated to contribute about 40% of the uncertainty range derived by NCRP (1997).

Because ICRP dose coefficients (values of dose per unit intake) are calculated as reference values using defined models and weighting factors, and apply to reference persons, they are not regarded as subject to uncertainty (ICRP 2007, Harrison and Streffer 2007). Thus, in general, regulatory compliance is determined using point estimates of effective dose with no consideration of uncertainties. An exception may be occupational exposures in which uncertainties are assessed for the exposure conditions. In such a case, a range on intake would result in a range on effective dose, calculated using reference dose coefficients. Similarly, uncertainties in effective doses to members of the public might be related to a probability distribution on concentrations of a radionuclide in a food material.

Full consideration of uncertainties will be of greater importance in applications such as the assessment of the probability of cancer causation for an individual and in estimating doses in epidemiological studies. While the ICRP system of protection does not take account of uncertainties, an understanding of the various contributions to uncertainty can be seen to be of value when making judgments on the optimisation of protection. For example, it may be appropriate to set up programmes of workplace monitoring to detect lower levels of exposure in situations where uncertainties in dose assessments are judged to be large. Similarly, assessments of uncertainties in doses to members of the public might be used to determine the fraction of a constraint at which concern would be raised. However, the routine consideration of uncertainties in dose assessments, if achievable, would be of questionable value when doses are generally maintained at small fractions of limits.

4. Summary and conclusions

This review provides a summary of and commentary on the methods recommended by the ICRP to quantify doses and risks from internal emitters, including consideration of uncertainties in these estimates. It is based on material published as chapter 2 (part 2) of the CERRIE (2004) report, but presents our interpretations rather than those of the whole CERRIE committee. Reference is also made to the new ICRP (2007) recommendations and other recent development. Two conclusions from CERRIE (2004) were that ICRP should clarify and elaborate its advice on the use of its dose quantities, equivalent and effective dose, and that more attention should be paid to uncertainties in dose and risk estimates and their implications.

The biokinetic and dosimetric models developed by ICRP over many decades (ICRP 1979, 2007) are intended primarily for the calculation of ICRP dose coefficients for the inhalation and ingestion of radionuclides—that is, values of committed equivalent dose and committed effective dose per Bq intake. However, the models have wider applications in the calculation of absorbed doses to organs and tissues in, for example, epidemiological studies and assessments of probability of cancer causation. Biokinetic models are being revised to take account of new experimental data and improve their ability to interpret bioassay data (Bailey et al 2007, Stather 2007). Dosimetric models are also being improved, using revised nuclear decay data (Endo et al 2004) and computational phantoms based on medical imaging data (Zankl et al 2007). The new generation of phantoms will provide better estimates of organ and tissue doses,
including a detailed representation of doses to target regions within individual bones of the skeleton (Bolch et al. 2007). These computational phantoms are well suited for applications in which adjustments are required to model the body shape and organ dimensions of specific individuals as, for example, in medical applications in which accurate estimates of absorbed doses are required.

The new ICRP (2007) recommendations provide explanation of the calculation and intended use of the protection quantities, equivalent and effective dose. The ICRP scheme provides a simple and convenient way of combining doses from different radiation types, from internal and external sources, for comparison with limits and other levels that relate to stochastic risks of whole-body exposure at low doses and dose rates. However, we emphasise that the radiation and tissue weighting factors used to calculate equivalent and effective dose are simplified values that do not reflect the complexities of the scientific data on which they are based. Equivalent and effective dose were not intended, and should not be used, as best estimates of dose relating to risk to specific individuals or population groups. The purpose of the ICRP methodology is primarily the regulatory control of radiation exposures and CERRIE (2004) agreed that the methodology fulfils this requirement. However, we also note that effective dose can conceal very different patterns of dose delivery from different radionuclides, both in the irradiation of specific tissues and in the time-course of dose delivery. Effective dose provides no information on risks of cancers of specific types, only of overall detriment relating to cancer and hereditary effects (ICRP 2007).

The limited human data that allow direct comparisons of cancer risks from internal emitters with the more comprehensive data for external radiation do not show large discrepancies, although uncertainties are large and are not readily quantifiable. Direct comparisons can be made for the induction of lung, liver and bone cancer and leukaemia by alpha-emitting radionuclides and external radiation (Harrison and Muirhead 2003, ICRP 2007). The greatest discrepancy was for leukaemia, although consistent results were obtained on the assumption of a low alpha particle RBE for this malignancy. Support for the direct comparison of doses from internal and external emitters is also provided by animal and in vitro data, comparing the effects of different radionuclides and external radiation (UNSCEAR 2000, WHO 2001). Uncertainties in the dose estimates for internal emitters in such studies need to be evaluated, but our overall conclusion is that the ICRP methodology for the assessment of doses from internal emitters is sufficiently good for the specified purposes. However, the wider application of the ICRP methods requires considerable care and justification.

CERRIE (2004) concluded that more efforts should be directed to quantification of uncertainties in dose estimates for important radionuclides, with transparent identification of all underlying contributions to overall uncertainties and how to compound them. The view was that doses and risks from internal emitters should be calculated on the basis of best current information using central values but that, where appropriate, these estimates should be accompanied by an explicit statement of the uncertainties involved. ‘This approach would help identify those situations in which a precautionary approach might be appropriate, and was greatly to be preferred over one in which conservative or pessimistic estimates were arbitrarily introduced at various stages in the calculation’. There are uncertainties associated with all aspects of the estimation of doses and risks at low doses and dose rates, in biokinetic and dosimetric models, in RBE data, and in risk coefficients. Assessments of uncertainties in risk estimates and in radionuclide doses have been published but there is as yet no comprehensive information on uncertainties for a range of radionuclides (CERRIE 2004, ICRP 2007). The importance of considering uncertainties where appropriate has been recognised by ICRP (2006, 2007). However, dose coefficients are published as point values without consideration of uncertainties.
Because ICRP dose coefficients (values of dose per unit intake) are calculated as reference values using defined models and weighting factors, and apply to reference persons, they are not regarded as subject to uncertainty (ICRP 2007). Thus, in general, regulatory compliance is determined using point estimates of effective dose with no consideration of uncertainties. Uncertainties in intake may be taken into account in a dose assessment, but not uncertainties in dose per unit intake. The use of constraints, and optimisation of protection below these levels, may be seen as a precautionary approach (NRPB 2004). We conclude that the ICRP approach is appropriate for general protection and regulatory purposes, and routine consideration of uncertainties, if it were possible, would introduce unwarranted complexity and not improve protection. However, we consider that the optimisation process should ideally be informed by knowledge of uncertainties, including an understanding of the various contributions to uncertainties in the assessment of doses and risks from internal emitters.

The CERRIE (2004) concern that ICRP should clarify and elaborate its advice on the use of its dose quantities, equivalent and effective dose, has been addressed by the explanations provided in the new ICRP (2007) recommendations. However, further elaboration of this advice is needed and we are aware that ICRP intend to issue additional guidance. Following the publication of the new recommendations, the next few years will see publications providing revised dose coefficients for radionuclide inhalation and ingestion and conversion coefficients for external radiation, introducing new and revised models as well as revised weighting factors. These coefficients will be published as single values without consideration of uncertainties. The issue of uncertainties is complex. It is clear that full consideration of uncertainties is appropriate when considering best estimates of doses and risks to individuals or specific populations groups. An understanding of the component uncertainties in the calculation of dose coefficients can be seen as an important goal and should help inform judgments on the optimisation of protection. The validity of assumptions made in the estimation of risks at low doses will continue to be challenged by advances in radiobiology and microdosimetry.

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